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(54) Phospholipid-containing composition, a process for its preparation and its use as an excipient for pharmaceutical substances.

(57) The invention relates to a solid phospholipid composition with a high phosphatidylcholine content which, in addition to the corresponding phospholipids, contains Palatinit and if appropriate one or more other auxiliaries, and a process for its preparation and its use as an oral presentation form.

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Phospholipid-containing composition, a process for its preparation and its use as an excipient for pharmaceutical substances

The invention relates to new phospholipid-containing compositions which, in addition to the corresponding phospholipids, contain Palatinit as a solidifying agent and if appropriate one or more auxiliaries, and a process for their preparation. The composition can be used as a solid oral presentation form.

Phospholipids occur widely in nature and can be obtained from animal and vegetable materials. The main sources are eggs (egg lecithin) and soya (soya lecithin), oil seeds and oil fruits, such as, for example, coconut-copra, palm kernels, groundnuts, rape, sunflower kernels, oil palms and olives. The phospholipids are predominantly obtained as a by-product in the production of vegetable oils. During this, a viscous mass is obtained by the so-called desliming of the vegetable oils, which is effected by passing small amounts of steam or water into the crude oil at elevated temperatures. This so-called lecithin slime has a varying composition, depending on its origin:

14 - 36 % by weight of vegetable oil
27 - 57 % by weight of water and
59 - 8 % by weight of phospholipids.

The commercially available crude lecithin is obtained by drying the lecithin slime in an evaporator at elevated temperatures (80 °C) over a relatively long period of time (from 6 - 12 hours) or at 100 °C in a thin film evaporator with a shorter residence time.

The most important crude lecithin is soya lecithin, which, after drying, contains about 52 % by weight of phospholipids, 35 % by weight of oils and fatty acids, 10 % by weight of glycolipids and sugars, 2 % by weight of non-hydrolysable portions and 1 % by weight of water.

The so-called de-oiled phospholipids (or de-oiled crude lecithin which contains only small amounts of oil and other concomitant lipids) are obtained by treatment with corresponding solvents, for example acetone. The lecithin fractions obtained have varying phospholipid compositions depending on their origin:

Soya lecithin:
about
30 % of phosphatidylcholine,
1 - 2 % of lysophosphatidylcholine,
22 % of phosphatidylethanolamine,
1 - 2 % of lysophosphatidylethanolamine,
3 - 4 % of phosphatidylserine,
18 % of phosphatidylinositol,
13 % of phytoglycolipids,
2 % of phosphatidic acid and
8 % of concomitant lipids. Egg lecithin:
73 % of phosphatidylcholine,
5 - 6 % of lysophophatidylcholine,
15 % of phosphatidylethanolamine,
2 - 3 % of lysphosphatidylethanolamine,
1 % of phosphatidylinositol,
2 - 3 % of sphingomyelin and
1 % of plasmologues.
Rape lecithin:
30 - 32 % of phosphatidylcholine,
3 % of lysophosphatidylcholine,
30 - 32 % of phosphatidylethanolamine,
3 % of lysophosphatidylethanolamine,
14 - 18 % of phosphatidylinositol,
1 % of lysophosphatidylinositol,
10 % of phytoglycolipids,
1 % of phosphatidic acid and
2 - 3 % of concomitant lipids.
Saflower lecithin:
32 - 39 % of phosphatidylcholine,
1 - 2 % of lysophosphatidylcholine,
14 - 17 % of phosphatidylethanolamine,

2 % of lysophosphatidylethanolamine,
21 - 27 % of phosphatidylinositol,
1 % of lysophosphatidylinositol,
15 - 28 % of concomitant lipids.

The individual lecithins can also be purified by known processes and the corresponding phospholipids can be separated into the individual constituents, such as phosphat.idylcholine, phosphatidylethanolamine, phosphatidylinositol, phosphatidylserine, phosphatidylglycerol, lysophosphatidylcholine, lysophosphatidylethanolamine, lysophosphatidylserine or lysophosphatidylglycerol, or olefinic mixtures can be prepared.

The phospholipid mixtures of very different composition, starting from wet lecithin slime, crude lecithin and de-oiled lecithin up to phospholipid mixtures of defined composition or even pure phospholipids, such as, for example, phosphatidylcholine, have physical properties which deviate very widely from one another. The phospholipid mixtures have a very different consistency from liquid to viscous-plastic. The plasticity of the lecithin increases with its degree of purity, that is to say as the phosphatidylcholine content increases and the oil content decreases.

Since lecithin and, to an increasing degree, highly pure lecithin are available, as is known, as a very highly viscous, paste-like composition, working already presents considerable difficulties because of the viscosity of the lecithin. The lecithin is difficult to meter, and because of its viscous consistency remains stuck to the equipment with which it comes into contact, so that the residues which remain require frequent and expensive cleaning of the equipment.

It is therefore often necessary to make do with preparing viscous or pasty preparations for the corresponding use from the crude lecithin by addition of auxiliaries.

If pure lecithin or particularly highly pure lecithin is used, the problem that the increasing purity of the lecithin results in the lecithin becoming increasingly sparingly soluble arises in particular.

The hygroscopic nature of the highly pure lecithin which renders mixing or coating of the highly pure lecithin with fat-like waxy substances practically impossible is a further hindrance.

Attempts have therefore often been made to convert lecithin into forms which allow easier processing.

Thus, U.S. Patent 2,057,695 describes a process for the preparation of powdered oil-free phosphatide products which have a very high lecithin content in the end product. In this process, crude phosphatide is de-oiled by extraction several times with acetone, water is added to the oil-free product, the residue of undissolved material is removed and the aqueous phosphatide emulsion which remains is further dried by spray drying or roller drying. Additions of sugar may be made here. The oil-free aqueous lecithin solution, which has a very high water content (about 20 to 50 times the amount), is then mixed directly with a stabilizer, such as, for example, salicylic acid, and can then subsequently be dried. If sugar is added, for example sucrose, a phospholipid content of a maximum of 60 % can be achieved.

U.S. Patent 3,012,888 describes oil-free phosphatide products which contain 1 - 5 % of monosaccharide and are obtained by adding a 40 % strength solution of corresponding monosaccharide to crude lecithin, heating the mixture to 60 - 70 °C until a homogeneous mass is obtained, subsequently drying the mass in vacuo and removing the oil with acetone. Finally, the residue solution is removed in vacuo. The aim of the application is the preparation of storage-stable phosphatide products starting from aqueous solution systems. If non-reducing sugars are used, no satisfactory results are obtained.

DE-PS 642,932 describes an industrial process for drying lecithin and subsequent coating with wax-like substances, whereas in DE-PS 973,741, drying by comminution under the influence of heat takes place, after de-oiling with acetone.

DE-PS 508,353 (U.S. Patent 1,776,721) contains technical instructions for mixing lecithin with flour or flour products.

U.S. Patent 1,988,050 describes a mixture of phospholipids crude (lecithin) and cereal germ which is de-oiled or dried with alcohol. In U.S. Patent 2,632,705, in addition to cereal flour, fatty acid esters are added to the lecithin.

In U.S. Patent 2,430,553, aqueous sugar solution is added to crude lecithin and the mixture is de-oiled and dried in a two-bath process. Products which have only a low lecithin content are obtained.

U.S. Patent 2,447,726 describes mixing of lecithin with gelose, a reducing sugar obtained form "Irish moss", and U.S. Patent 2,708,631 describes a solution of a maximum of 20 % of lecithin in dextrose.

U.S. Patent 2,973,381 describes a composition of phospholipid and tocopherol (vitamin E) whereas in U.S. Patent 3,480,544 phospholipids and SiO_2 are mixed with one another.

In U.S. Patent 2,929,723, liquid aromatics are converted into solid products with the aid of lecithin (0.1 - 5 %).

All the previous processes have the disadvantage that either only small lecithin contents are present in

the product or expensive product preparation is necessary. In addition, the consistency of the product is often unsatisfactory.

The aim of the present invention is therefore to discover an additive and a method with which phospholipid mixtures from different starting substances are converted into products which can also have a high phosphatidyl-choline content and the consistency of which can be controlled by the choice of additive and its amount.

This object is achieved by a phospholipid-containing composition which contains sugar as a solidifying agent and customary auxiliaries, characterized in that a 1:1 mixture of glucopyranosido-1,6-mannitol and glycopyranosido-1,6-sorbitol (Palatinit) in a weight ratio of phospholipid:Palatinit of 1:20 to 20:1 is present as the sugar.

Surprisingly, it has now been found that it is possible to mix Palatinit, a non-reducing sugar, with highly pure lecithin and in this way to obtain products which have an extremely solid consistency and are not sticky.

It is also completely surprising that Palatinit and lecithin can be mixed with one another directly, without the customary antiadhesives, and the sticky properties of the lecithin and its strong hygroscopic character, which is otherwise a great hindrance to effective processing, can be neutralized completely by means of the Palatinit, so that solid stable products which are very easy to handle are formed in a one-stage process. The consistency of the product can be controlled here from pasty to very solid via the ratio of Palatinit to phospholipid. The weight ratio of phospholipids:Palatinit is 1:20 to 20:1, preferably 4:1 to 20:1.

Palatinit is a non-reducing sugar and the trade-name for a hydrogenated isomaltulose which consists of a 1:1 mixture of glucopyranosido-1,6-mannitol and glucopyranosido-1,6-sorbitol and has a purity of >99 % (J.S. Hoeven, Caries Res., 13 (1979), page 301).

The composition can contain naturally occurring or synthetic phospholipids.

All products in which the phospholipid content can vary from 5 to 98 %, such as, for example, egg lecithin (about 80 % of phosphatidylcholine, the remainder being other phospholipids), soya lecithin (about 77 % of phospholipids, 13 % of phytoglycolipids, 2 % of phosphatidyl acid and 8 % of concomitant lipids) or highly pure phospholipids having a phosphatidylcholine content of up to 96 %, can be employed as the phospholipid-containing starting mixtures. Phospholipid mixtures of different composition can likewise also be employed. The phospholipid fractions can be obtained from soya beans, rape, sunflower kernels and other oil fruits and oil seeds, but preferably from soya beans, by processes which are known per se in accordance with DE-OS 30 47 048, DE-OS 30 47 012 and DE-OS 30 47 011.

Auxiliaries which can be employed, for example for improving the taste, are the customary aroma substances, such as, for example, vanillin, aniseed, caramel, chocolate, malt, peppermint oil or fruit aromas, such as, for example, banana, orange, raspberry or mixtures thereof.

Sweeteners, for example sodium cyclamate, saccharin, xylitol, cane sugar (sucrose), glucose, fructose or maltose or other sweetener derivatives, can likewise also be used. It is also possible to combine several of the abovementioned auxiliaries, in order thus to be able to prepare the composition of desired taste. The amount of auxiliaries in the composition can be up to 5 % by weight, based on the total weight. The products can be processed by customary methods into grains, granules, bars, chewable tablets and the like, or converted into other forms which allow further processing without problems.

The mixture of lecithin or phospholipid/Palatinit can be prepared by producing a lecithin solution, mixing this with the corresponding amount of Palatinit or Palatinit solution and subsequently freeing the mixture from adhering solvent in a roll mill drier or spray drier.

Surprisingly, however, it is also possible to prepare the composition by adding a melt of Palatinit to lecithin or phospholipids under the influence of heat and mixing the components by customary methods until a homogeneous mass has formed. The customary aroma substances, such as, for example, vanillin, aniseed, caramel, chocolate, malt, peppermint oil or fruit aromas, such as, for example, banana, orange, raspberry or mixtures thereof, can then be added to this homogeneous phase.

It is also possible to add sweeteners, for example sodium cyclamate, saccharin, xylitol, cane sugar (sucrose), glucose, fructose or other sweetener derivatives or corresponding combinations.

After its homogenization, the entire mass can be shaped under plastic conditions under the influence of heat or, after cooling, processed to grains, granules, bars, tablets and the like, or converted into other forms which allow further processing without problems.

The composition is plastic at temperatures from 50 °C to 80 °C, so that it is preferable to prepare the composition at these temperatures by mixing the constituents, and also to convert it into oral presentation forms. The composition is preferably used as an oral presentation form. It can in this way also serve as an excipient for medicaments for oral administration, that is to say pharmaceutically active substances.

Oral presentation forms are, for example, granules, tablets, chewable tablets, bars/toffees, film-coated

tablets and filled hard gelatin capsules.

The invention is described in more detail by the following examples:

Example 1

Purified soya lecithin (about 76 % of phosphatidylcholine)	3947 g
Palatinit	2008 g
Vanillin	45 g

The purified soya lecithin is kneaded at 80 °C in the customary manner and the hot Palatinit mass at 140 °C is added. When the mixture has reached a temperature of 80 °C vanillin is added and the mixture is kneaded until a homogeneous mass has formed. The product can be shaped under plastic conditions under the influence of heat or, after cooling, processed to grains, granules, bars, chewable tablets and the like, it also being possible to incorporate pharmaceutically active substances, if appropriate, so that the composition is used as an excipient.

Example 2

Purified soya lecithin (about 76 % of phosphatidylcholine)	6579 g
Palatinit	3346 g
Vanillin	75 g

Preparation analagous to Example 1.
A solid product is formed.

Example 3

Purified soya lecithin (about 76 % of phosphatidylcholine)	2831 g
Palatinit	1145 g
Vanillin	24 g

Preparation analagous to Example 1.
A solid product is formed.

Example 4

Purified soya lecithin (about 76 % of phosphatidylcholine)	3875 g
Palatinit	1078 g
Vanillin	47 g

Preparation analagous to Example 1.
A solid product is formed.

Example 5

Purified soya lecithin (about 76 % of phosphatidylcholine)	118.5 g
Palatinit	10.0 g
Vanillin	1.5 g

Preparation analagous to Example 1.
A mass which has very viscous, pasty properties but is not sticky is formed.

Example 6

Highly pure phospholipids (about 98 % of phosphatidylcholine)	75.27 g
Palatinit	23.98 g
Vanillin	0.75 g

Preparation analagous to Example 1.
A solid product is formed.

Example 7

Highly pure phospholipids (about 98 % of phosphatidylcholine)	57.57 g
Palatinit	41.73 g
Vanillin	0.70 g

Preparation analagous to Example 1.
A solid product is formed.

Example 8

Highly pure phospholipids (about 98 % of phosphatidylcholine)	81.41 g
Palatinit	18.11 g
Vanillin	0.48 g

Preparation analagous to Example 1.
A solid product is formed.

Example 9

Highly pure phospholipids (about 98 % of phosphatidylcholine)	90.25 g
Palatinit	9.01 g
Vanillin	0.74 g

Preparation analagous to Example 1.
A product which has a very viscous, pasty consistency but is not sticky is formed.

Example 10

Highly pure phospholipids (about 98 % of phosphatidylcholine)	92.43 g
Palatinit	7.02 g
Vanillin	0.45 g

Preparation analagous to Example 1.
The product has the same properties as in Example 9.

Examples 11 to 15

These correspond to Examples 1 to 5, but the vanillin is replaced by the same amount of xylitol and vanillin in the ratio 1 : 1. Products with the same properties as in Examples 1 to 5 are obtained.

Examples 16 to 20

These correspond to Examples 6 to 10. The vanillin is replaced by the same amount of aniseed. Products with the properties of Examples 6 to 10 are formed.

Example 21

Phospholipid-Palatinit product (for example from Example 2 or 12)	1440 g
Powdered Palatinit	315 g
Silicon dioxide	45 g

The finished solid product from Example 2 is ground to free-flowing granules by customary processes and the granules are then mixed with the Palatinit powder and the SiO_2. Chewable tablets having a diameter of 16 mm (weight 1.5 g) and those having a diameter of 22 mm (weight 2.5 g) are pressed in a customary tablet press.

Example 22

Phospholipid-Palatinit product	**800 g**

(for example from Example 2 or 12)	
Powdered Palatinit	160 g
Silicon_dioxide	25 g
Caramel aroma	15 g

Preparation of chewable tablets analogous to Example 21.

Example 23

Phospholipid-Palatinit product (for example from Example 2 or 12)	527 g
Powdered Palatinit	160 g
Silicon dioxide	25 g
Finely powdered glyceride mixture	15 g

Preparation of chewable tablets analogous to Example 21.

Example 24

Phospholipid-Palatinit product (for example from Example 2 or 12)	777 g
Powdered fructose	117 g
Silicon dioxide	25 g
Powdered cacao	75 g
Vanillin	6 g

Preparation of chewable tablets analogous to Example 21.

Example 25

Phospholipid-Palatinit product (for example from Example 2 or 12)	777 g
Powdered Palatinit	72 g
Powdered fructose	10 g
Silicon dioxide	25 g
Cream aroma	20 g
Vanillin	6 g

Preparation of chewable tablets analogous to Example 21.

For Examples 26 - 29, a soya lecithin of the following composition was used: 35 % of phosphatidylcholine, 26 - 33 % of other phospholipids and other concomitant substances and 32 - 39 % of oil.

Example 26

Lecithin (35 % of phosphatidylcholine)	715 g
Palatinit	1760 g
Vanillin	25 g

Example 27

Lecithin (35 % of phosphatidylcholine)	1072 g
Palatinit	1403 g
Vanillin	25 g

Example 28

Lecithin (35 % of phosphatidylcholine)	3500 g
Palatinit	2440 g
Vanillin	60 g

Example 29

Lecithin (35 % of phosphatidylcholine)	3330 g
Palatinit	630 g
Vanillin	40 g

The products of Examples 26 - 29 are solid.
For Examples 30 to 33, in each case one of the compositions shown below is used.

Composition I

Highly purified phospholipids (up to 98 % phosphatidylcholine)	1400 g
Palatinit	600 g

Composition II

Purified soya lecithin (about 76 % of phosphatidylcholine)	1400 g
Palatinit	600 g

Composition III

Lecithin (35 % of phosphatidylcholine)	1400 g
Palatinit	600 g

Example 30

(Lecithin-multivitamin chewable tablets)

1.	Base (I, II or III)	1944.00 mg
2.	Vitamin A, 500,000 IU/g (retinolacetate)	4.00 mg
3.	Vitamin B_1 (thiamine chloride . HCl)	0.25 mg
4.	Vitamin B_2 (riboflavin)	1.00 mg
5.	Vitamin B6 (pyridoxine . HCl)	1.00 mg
6.	Vitamin B12 (cyanocobalamine)	1.00 µg
7.	Vitamin C	50.00 mg
8.	Vitamin D, 100,000 IU/g (colecalciferol)	2.00 mg
9.	Vitamin E (50 %) (tocopherol acetate)	1.00 mg
10.	Nicotinamide	10.00 mg
11.	Folic acid	0.25 mg
12.	Palatinit PF	556.00 mg
13.	Vanillin DAB 8	17.00 mg
14.	Kollidon 25	143.00 mg
15.	Syloid 244	29.00 mg
16.	Sodium chloride	0.60 mg
17.	Aerosil R 972	29.00 mg
18.	Aspartame	0.60 mg
19.	Stearic acid	57.00 mg
20.	Apricot aroma	14.50 mg

The substances are mixed together and pressed to biplanar chewable tablets having a diameter of 25 mm and a weight of 2.86 g with the aid of a tablet press.

Example 31

(Lecithin-multivitamin-mineral chewable tablets)

The following substances are also added to the mixture from Example 1:

1.	Copper(II) sulphate	0.50 mg
2.	Manganese(II) sulphate	0.20 mg
3.	Iron(II) sulphate	20.00 mg
4.	Cobalt(II) sulphate	0.40 mg
5.	Magnesium carbonate	20.00 mg
6.	Zinc oxide	0.05 mg
7.	Calcium hydrogen phosphate	98.85 mg

This entire mixture is then pressed to biplanar chewable tablets having a diameter of 25 mm and a weight of 3.0 g with the aid of a tablet press.

Example 32

(Lecithin-containing antacid chewable tablets)

1.	Base (I, II or III)	1000.00 mg
2.	Alugel (dried aluminium hydroxide gel, Giulini-Chemie, Ludwigshafen)	505.00 mg
3.	Palatinit PF	407.00 mg
4.	Skimmed milk powder	500.00 mg
5.	Sodium cyclamate	3.00 mg
6.	Kollidon 25	50.00 mg
7.	Syloid 244	20.00 mg
8.	Peppermint essence	5.00 mg
9.	Magnesium stearate	10.00 mg

The base is mixed with the Alugel granules and other substances and the mixture is then pressed to chewable tablets weighing 2.5 g.

Example 33

1.	Base (I, II or III)	1000.00 mg
2.	Wheat bran	1000.00 mg
3.	Palatinit PF	500.00 mg
4.	Syloid 244	35.00 mg
5.	Kollidon 25	150.00 mg
6.	Aerosil R 972	25.00 mg
7.	Aspartame	0.70 mg
8.	Vanillin DAB 8	20.00 mg
9.	Stearic acid	60.00 mg

Bars of various sizes are produced with this mixture.

In order to demonstrate the superiority of Palatinit as a solidifying agent over known sugars, comparison experiments are carried out.

Tabletting experiments were carried out with granules which contained lecithin carbohydrate and have been obtained by mixing the solid starting substances. The granules were obtained by means of a AMK kneader or Berstorff extruder. After mixing the granules with the auxiliaries listed, the tablets were pressed in a bi-planar stamp form of 25 mm diameter in a tablet press of the type Hillian RT 116.

The following amounts of substances were used for all the experiments:

Purified soya lecithin: (phosphatidylcholine content of about 76 %)	55.65 g
Carbohydrate:	23.85 g
Tabletting auxiliaries	
Avicel PH:	20 g
Aerosil 200:	0.50 g
Stearic acid (optional):	3 g
(if stearic acid is used, only 17 g of Avicel PH are employed).	

The results can be found in Table 1 (without addition of stearic acid) and in Table 2 (with addition of stearic acid):

Table 1

	Carbohydrate				
	Glucose	Fructose	Xylitol	Mannitol	Palatinit
Effect sticking to tablet stamps	yes	yes	yes	yes	no
"Capping" of the tablets	yes	yes	yes	no	no
Pressing possible	no	no	no	no	yes

"Capping" of the tablets means that these disintegrate into two flat (cap) halves on leaving the pressing die. A yes in this column leads to a devaluation of the properties.

Table 2

(with addition of stearic acid)	Carbohydrate				
	Glucose	Fructose	Xylitol	Mannitol	Palatinit
Effect sticking to tablet stamps	yes	yes	yes	yes	no
"Capping" of the tablets	no	no	yes	no	no
Pressing possible	no	no	no	no	yes

The superiority of the product according to the invention of lecithin plus Palatinit can be clearly seen from the results, since this mixture is the only one which leads to non-sticking forms which can be pressed.

Claims

1. Phospholipid-containing composition which contains sugar as a solidifying material and customary auxiliaries, characterized in that a 1:1 mixture of glucopyranosido-1,6-mannitol and glycopyranosido-1,6-sorbitol (Palatinit) in a weight ratio of phospholipid:Palatinit of 1:20 to 20:1 is present as the sugar.

2. Phospholipid-containing composition according to Claim 1, characterized in that it contains naturally occurring or synthetic phospholipids as the phospholipids.

3. Phospholipid-containing composition according to Claims 1 to 3, characterized in that it contains soya lecithin or egg lecithin or a highly purified fraction thereof as the naturally occurring phospholipids.

4. Process for the preparation of a phospholipid-containing composition which contains sugar as a solidifying agent and customary auxiliaries, characterized in that Palatinit is introduced in a weight ratio of phospholipids:Palatinit of 1:20 to 20:1, the phospholipids being mixed with a melt of Palatinit under the influence of heat until the mixture is homogeneous and the product being comminuted, after cooling.

5. Use of the phospholipid-containing composition according to Claims 1 - 4 as an oral presentation form.

6. Use according to Claim 6, characterized in that the composition serves as an excipient for pharmaceutically active substances for oral administration.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 89 11 4144

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
D,A	US-A-3 012 888 (P.F. DAVIS) * claims 1-5; examples 1-5 * ---	1-6	A 23 J 7/00 A 61 K 9/20
A	EP-A-0 072 469 (R. HOCHSCHILD) * Claims 1-2; example * ---	1-3,5-6	
A	CHEMICAL ABSTRACTS, vol. 109, no. 19, 1988 abstract no. 169028v, Columbus, Ohio, US; M. NAKANISHI: "Sweetness of palatinit and its use in foods", & GEKKAN FUDO KEMIKARU, 4(6), 81-6 * Abstract * ---	1,5	
A	CHEMICAL ABSTRACTS, vol. 104, no. 10, 1984, abstract no. 74837r, Columbus, Ohio, US; & JP-A-60 204 710 (LION CORP.) 16-10-1985 * Abstract * -----	1	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A 23 J
A 61 K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	18-10-1989	SANTOS Y DIAZ A.I.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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